Bandolier 53

What do we think?
What do we know?
What can we prove?

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HEALTH AND EFFICIENCY

Health & Efficiency was the title of an old-fashioned magazine whose main claim to fame was that it was the only place to see pictures of semi-naked people before such pictures arrived with the cornflakes. Sex and money are two of the major drivers for human behaviour. For income taxes there is something called the Laffer curve: when the income tax rate is zero, the tax collected is zero, but when the tax rate is 100% the tax take is also zero. Somewhere in between is an area where tax collected is maximised because people are willing to pay it without using elaborate avoidance behaviour.

No laughing matter

When ***Bandolier*** first visited the topic of erectile dysfunction someone wrote in and asked if we were joking - surely this wasn't a serious topic for the NHS. We had checked on this, and found a pharmacist struggling with a request for seven intercavernosal injections a week. It is a serious matter, undoubtedly with evidence overtones, but with even more serious questions about access and payment. We can't deal with the latter, but perhaps we can inform on the former.

Fads and epidemiology

In the last year or so ***Bandolier*** has reported on various aspects of healthy living and healthy lifestyles. Some have been one or more good studies in a particular area, others, like this month on page 8, systematic reviews and meta-analysis. The striking feature is how good the evidence often is, and how big some of the effects are.

The Devil, it seems, does not have all the good tunes. Yet every time ***Bandolier*** talks to someone about healthy living issues, they make the point that no-one seems to make best use of it. Why not? Don't ask ***Bandolier***, because we don't know. But we would be interested if we are missing really good books, or leaflets, or other information for doctors and patients on the topic of healthy living.

In this issue

ERECTILE DYSFUNCTION

Bandolier 43 raised the issue of treatments for erectile dysfunction. At that time only one study in 12 men was available on the new oral treatment, sildenafil [1]. Two new studies in much larger populations are now available for assessment of sildenafil in more detail [2].

Measuring erectile dysfunction

The basic method used in the sildenafil study was that of a self-administered measure of erectile dysfunction, the international index of erectile dysfunction (IIEF) [3]. The importance of this instrument is that it has been developed to examine the main features of erectile dysfunction, is quick and simple to complete, and has the sensitivity and specificity to detect treatment-related changes in erectile dysfunction. It has 15 questions, easily scored, and is likely to be a useful diagnostic aid in erectile dysfunction.

The key features of the scale and its development were:

- 15 questions dealing with erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction.
- Based on literature search of existing questionnaires.
- Developed from an initial questionnaire after trials with patients and review by an expert panel.
- Validated in ten languages.
- Examined for validity in a number of contexts.

The full questionnaire is a bit too long for the pages of ***Bandolier***, but is given in an appendix in the paper [3].

Sildenafil efficacy 1

The first study was a double-blind dose-response design in which men were randomly assigned placebo (216 men) , or 25 mg (96), 50 mg (105), or 100 mg (101) of sildenafil one hour before planned sexual activity (and not more than once daily). For inclusion, men had to be in a stable relationship of more than six months' duration. They had to have erectile dysfunction of organic, psychogenic, or mixed origin. Exclusions included men with penile anatomical defects, another sexual disorder, spinal cord injury, major psychiatric disorder, poorly controlled diabetes, or stroke, or myocardial infarction within six months, or use of organic nitrates.

Results

The mean age was 58 years, about 80% had organic causes of erectile dysfunction for an average of 3 years, and about 28%

had hypertension, 18% hyperlipidaemia, 14% diabetes, 11% radical prostatectomy and 8% ischaemic heart disease. Results on efficacy were taken from questions 3 ("When you attempted sexual intercourse, how often were you able to penetrate your partner?") and question 4 ("During sexual intercourse, how often were you able to maintain an erection after you had penetrated your partner?") of the IEFF index.

There was a dose-response with sildenafil (Figures). With doses of 50 and 100 mg there was a change from erections rarely adequate for penetration and rarely maintained to erections being both adequate and maintained much more than half the time. The effectiveness of sildenafil was broadly similar for men whose erectile dysfunction had an organic, psychogenic or mixed cause.

Sildenafil efficacy 2

A second study enrolled 329 different men who were randomly assigned to placebo (160 men) or 50 mg sildenafil (163 men) for 12 weeks. At follow up visits the dose could be doubled, or reduced by 50% on the basis of effectiveness and adverse effects.

Results

During the last four weeks of treatment the mean number of successful attempts at sexual intercourse was 5.9 with sildenafil, compared with 1.5 with placebo. Successful sexual intercourse occurred in 69% of attempts with sildenafil and 22% with placebo. Improved erections were reported by 101 of 136 men taking sildenafil and 23 of 118 taking placebo. This gives a number needed to treat of 1.8 (95% CI 1.5 to 2.3).

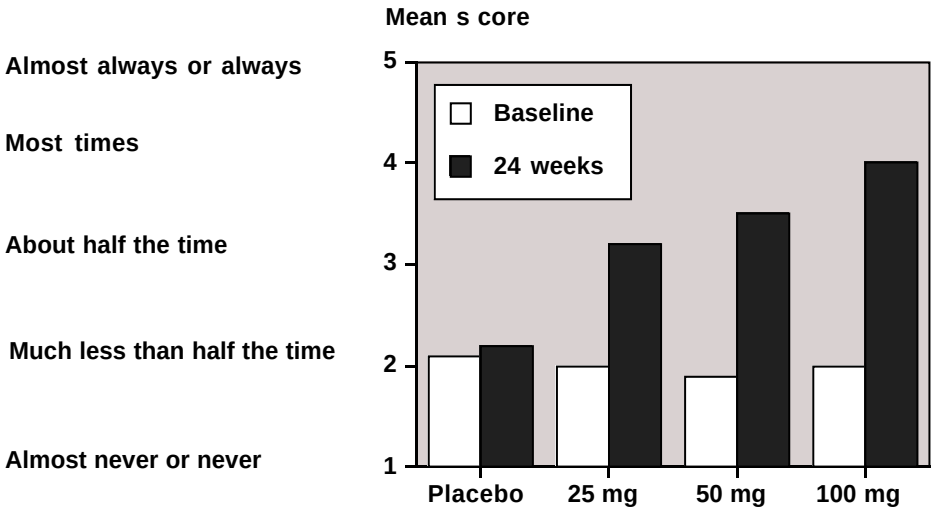
Adverse effects

Use of sildenafil was associated with some adverse effects In the first Table adverse effects from both studies [2] and all doses are combined, though most showed a dose-response. The main adverse effects reported were flushing, headache, dyspepsia, visual disturbance (changes in perception of colour hue or brightness) and rhinitis. These were mild, and the number of discontinuations because of adverse effects was small at 5 of 479 patients (<1%).

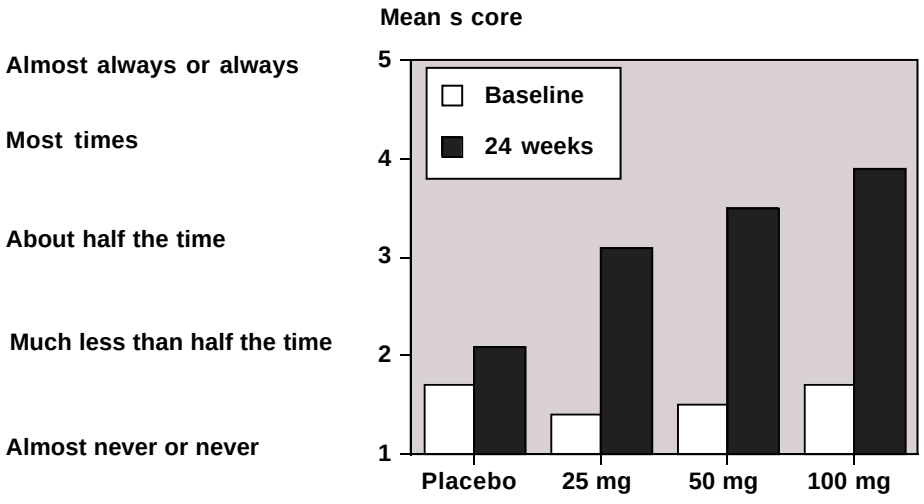
A more complete picture of adverse events comes from an analysis of all randomised and double blind placebo controlled studies, together with open label extensions [4]. The second Table extracts the information on the 1500 men given sildenafil or placebo in flexible dose studies, those most likely to reflect drug use in practice. The adverse effect incidence is only slightly different. Over 90% of these adverse effects were mild or moderate, and adverse effect discontinuations in these studies was just over 2% for both placebo and sildenafil. There were no cases of priapism in any of the studies.

Because the men who will be prescribed sildenafil will have cardiovascular risk factors, like hypertension, hyperlipidaemia and diabetes, the drugs's effect on cardiovascular events is very important. An analysis of all 18 placebo-controlled trials showed no difference in the incidence of myocardial infarction, angina or coronary artery disorders between sildenafil use and placebo (4274 men), nor was the incidence higher in the 2199 men taking part in open-label extensions (third Table). Blood pressure and heart rate were unaffected.

Sildenafil: 24 weeks treatment and effect on penetration



Sildenafil: 24 weeks treatment erection maintenance



Comment

Here we have some well-conducted and large randomised trials which show good efficacy for important outcomes, together with a sensible portrayal of possible harm. The evidence so far is that sildenafil is effective, and safe. The men in the effectiveness study [2] had an average age of 58 years, and the majority had conditions associated with erectile dysfunction, and will represent a significant proportion of men with erectile dysfunction. The obvious missing group was men with spinal inju-

Sildenafil adverse effects: combined studies and doses

	Placebo (N=382)	Sildenafil (N=479)	Number needed to harm (95%CI)
Adverse effect			
Flushing	4	93	5.4 (4.5 to 6.8)
Headache	20	99	6.5 (5.1 to 9.0)
Dyspepsia	7	41	15 (10 to 26)
Visual disturbance	2	22	24 (16 to 49)
Rhinitis	5	24	27 (17 to 69)
Discontinuations			
Inadequate response	14	6	
Treatment-related	2	5	

Sildenafil adverse effects in PRN flexible-dosing studies

Adverse effect	Placebo (N=725)	Sildenafil (N=734)	Number needed to harm (95%CI)
	Percent		
Headache	4	16	8.4 (6.7 to 11)
Flushing	1	10	11 (8.9 to 15)
Dyspepsia	2	7	20 (14 to 36)
Rhinitis	2	4	53 (28 to 753)
Visual disturbance	0	3	33 (23 to 56)
Diarrhoea	1	3	49 (29 to 165)

Adverse effects were mild or moderate in 92% of cases

Incidence of serious cardiovascular events in Phase II/II studies

Studies	Incidence (95% CI) Placebo	Sildenafil
Phase II/III placebo-controlled		
Serious cardiovascular events	5.7 (3.3 to 8.2)	4.1 (2.7 to 5.5)
Myocardial infarction	1.4 (0.2 to 2.6)	1.7 (0.8 to 2.6)
Pase II/III open-label extensions		
Serious cardiovascular events		3.5 (2.3 to 4.7)
Myocardial infarction		1.0 (0.3 to 1.6)

Serious adverse events includes myocardial infarction, angina and coronary artery disorders

ries, though abstracts of as-yet unpublished studies indicate that sildenafil is just as effective in them.

Treatment efficacy for oral sildenafil is about the same (NNT of about 2) as for intracavernosal injection or intraurethral application of alprostadil (***Bandolier*** 43). Adverse effects are different. Intraurethral alprostadil was associated with some mild pain (NNH 3.5), mild urethral trauma (NNH 25) and dizziness (NNH 50).

Because sildenafil's mode of action potentiation of hypotensive effects of nitrates is expected, and apparently was demonstrated in early studies. Use of sildenafil in men using organic nitrates is therefore contraindicated.

Clearly the advent of several new and effective treatments for male erectile dysfunction poses some difficult questions about who gets what treatment and when. And given that there is a large, and largely unmet, need, in an area that has caught the public (or at least the media) imagination, some thinking caps will be necessary to work out the most appropriate way to deal with what experience in the USA and elsewhere suggests might be an insatiable demand.

References:

1 M Boolell, S Gepi-Attee, JC Gingell, MJ Allen. Sildenafil, a novel effective oral therapy for male erectile dysfunction. British Journal of Urology 1996 78: 257-61.

2 I Goldstein, TF Lue, H Padma-Nathan et al. Oral sldenafil in the treatment of erectile dysfunction. New England Journal of Medicine 1998 338: 1397-1404.

3 RC Rosen, A Riley, G Wagner et al. The international index of erectile dysfunction (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 199749: 822-30.

4 A Morales, C Gingell, M Collins et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. International Journal of Impotence Research 1998 10: 69-74.

Fluoride gel and caries

The prevalence of caries in children in many countries in Western Europe and North America has declined dramatically in the last few decades. Reasons for this include the widespread use of fluoride toothpastes, and, in some cases, fluoridation of water supplies.

Additional use of fluoride gels with high fluoride contents has been one method of reducing tooth decay. These gels use higher concentrations and different formulations of fluoride from those found in most toothpastes. There are various forms of application, applied by individuals or by professionals, at a frequency from once a day to once a year. And they are used in populations with caries prevalence which might be low or very high.

Is the use of fluoride gels effective, and what amongst all these factors is important? A new meta-analysis [1] gives some answers.

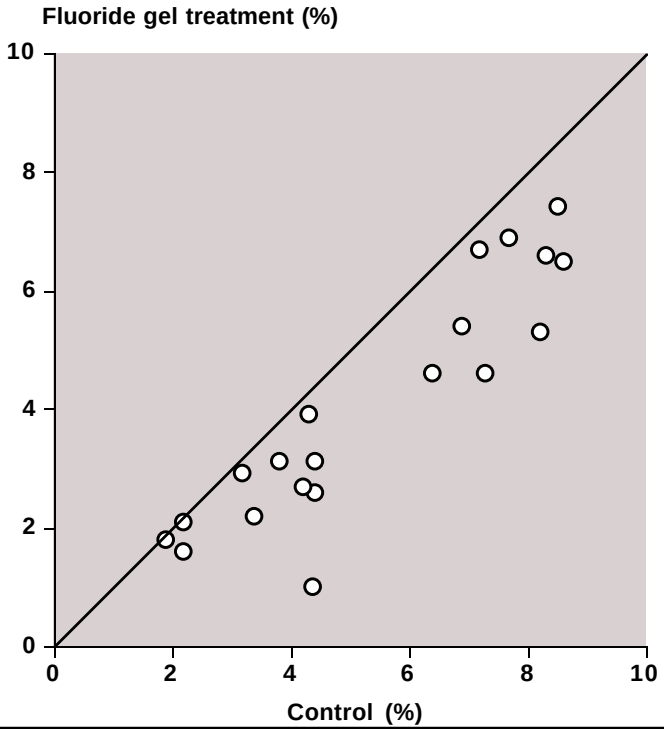
Review

The review sought randomised studies in populations representative of the general population on fluoride gels applied to permanent teeth of children aged six to 15 years. Only English and German studies published between 1965 and 1995 were used, and only MEDLINE searched.

Results

Twenty-four studies were found, with a wide variation in the number of decayed, missing and filled surfaces (DMFS) at baseline (means 0.8 to 10.1) and application frequency (1 to 360 times per year). Follow-up periods were 1.5 to 3 years (median 3 years). Studies were large, with only a three studying fewer than 200 children.

Incidence of decayed, missing and filled surfaces at follow-up



The overall caries-inhibiting effect was 22% (95% CI 18 to 25%). This was a consistent effect at all levels of incidence of DMFS, as the L'Abbé plot shows. There was no effect of type of gel, or number of applications.

The most interesting part of the paper was the calculation of numbers needed to treat at various levels of background prevalence, using the consistent 22% effect.

Background caries incidence (DMFS/year)	NNT for one year treatment (95% CI)
0.25	18 (16 to 22)
0.50	9.1 (7.8 to 11)
1.00	4.5 (3.9 to 5.4)
1.50	3.0 (2.6 to 3.6)

Comment

The NNT is low at high DMFS incidence for even one year of treatment, and there is an interesting discussion in the paper about how this could impact on cost-effectiveness strategies for reducing tooth decay in children. It might well make it easier to justify targeting efforts into areas of high prevalence, perhaps as part of a health improvement programme. It is also great to see dentists using NNTs.

Bandolier consults a wise old dentist, who makes the point that the issue of caries in children is not the only topic about which we need information on fluoride gels. There is a second wave of tooth problems in the elderly, and determining whether fluoride gels are useful in this setting is a priority. So far searching for a review has brought nothing forth, but perhaps young, keen, research dentists know of one.

Reference:
1 HM van Rijkom, GJ Truin, MA van't Hof. A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. Caries Research 1998 32: 83-92.

Beyond the basics?

2nd Symposium on Systematic Reviews: Beyond the Basics
5th-7th January 1999
St Catherine's College, Oxford, UK

Call for abstracts, deadline 4 September 1998

Further information from Rochelle Seifas, Centre for Statistics in Medicine, Institute of Health Sciences, Old Road, Headington, Oxford, OX3 7LF, UK.
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More on NSAIDs

In ***Bandolier*** 52 we examined some of the problems associated with NSAID use. Since then two reports which cast additional light on the UK situation have swum into our ken.

Burden in the UK

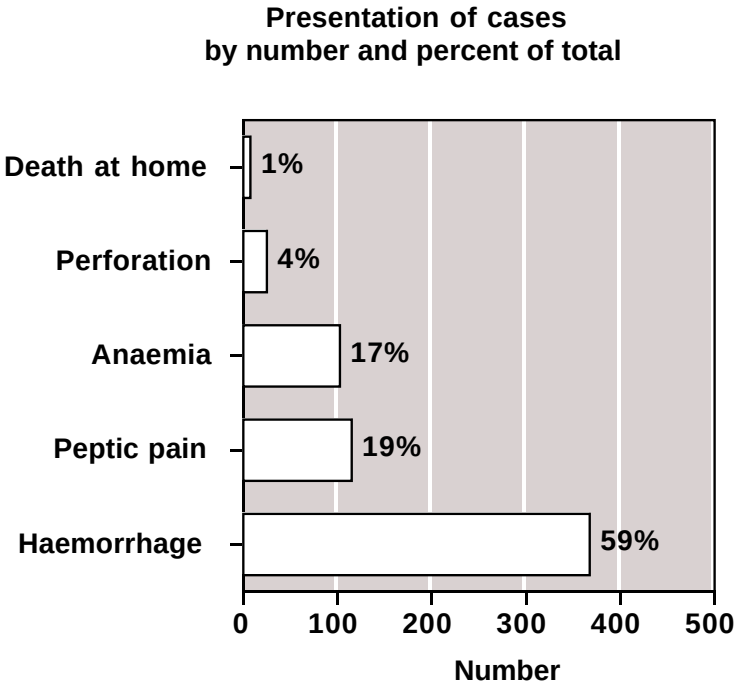
How big is the problem in the UK? A retrospective case-control survey of emergency admissions for upper gastrointestinal disease in two English general hospitals covering 1% of the UK population (in Rotherham and Stockport) gives some good estimates [1]. Records of all community deaths attributed to upper gastrointestinal disease were also surveyed. Matched controls were identified from emergency admissions for other causes.

There were 620 emergency admissions over one year in 1990/91, with controls for 460 cases. Controls were matched for GP practice, sex, age, and date of admission. Unmatched cases were retained in the analysis.

Results

Cases and controls were well matched, except for musculoskeletal disease (24% vs 3%). Cases were more likely to be using NSAIDs (31% vs 16%), H2-receptor antagonists (20% vs 5%), ferrous sulphate (9% vs 2%) and prednisolone (7% vs 3%).

Cases presented largely (59%) as haemorrhage (Figure), with a small proportion presenting as perforation, and 1% dying at home. Blood transfusion was required in 36% of all cases, and in 50% of those taking NSAIDs. NSAID users needed significantly more blood transfused than non-users. NSAID users also required a significantly longer stay (24% had a hospital stay of more than 14 days). NSAID users were more likely to die: overall mortality was 20% in NSAID users compared with 14% in non users.



Extrapolation to the UK

These results suggest an overall incidence of upper gastrointestinal emergencies in the UK of 147 per 100,000 of the adult population, with an incidence of gastrointestinal haemorrhage of 87/100,000. This would indicate about 65,000 such crises a year in the UK. The study estimated that 1.9% of NSAID users in the Rotherham and Stockport area were admitted to hospital each year with upper gastrointestinal emergencies. The NSAID-attributable number of NSAID-associated emergency admissions in the UK would be about 12,000, with about 2,500 deaths.

Prescribing consequences

Another study in Nottingham [2] prospectively interviewed 500 patients over 60 years admitted to the city's two hospitals with peptic ulcer bleeding over a five year period. A structured questionnaire was used to determine NSAID use. General practice prescribing was also examined for patients admitted, looking at 103 general practices responsible for half a million people.

Results

Overall NSAID prescribing varied greatly, by about six-fold from lowest to highest prescribing practices, even when patient mix was taken into account. Raw prescribing rates were between 137 items per 1000 population and 833 items per 1000.

The average admission rate for bleeding peptic ulcer was 15 per 100,000 per year. Analysis indicated a 0.23% (95%CI 0.08 to 0.31%) increase in the rate of ulcer bleeding of all causes in the elderly for each increase of 1 NSAID prescription per 1000 patients. This is equivalent to one episode of ulcer bleeding in the elderly per 2,823 (95%CI 2095 to 8116) prescriptions.

Comment

These two papers provide real data for the health economists to get their teeth into in order to show us what the costs associated with NSAID gastrointestinal effects truly are, and how that can inform best prescribing practice. A simple back-of-an-envelope calculation can tell us that if we guess the cost of an admission for bleeding peptic ulcer to be £5,600, this would mean an additional adverse-effect cost of £2 per NSAID prescription - more perhaps than the cost of the drug. It might be much higher when all-cause hospital admissions are taken into account.

The observation of a six-fold variation in GP prescribing rates, even when corrected for case-mix, is interesting. It suggests that better guidelines are needed.

Moreover

NSAID prescribing is interesting and important area which can constitute a significant portion of prescribing budgets. ***Bandolier*** 51 contained an item which suggested that filling knowledge gaps needed three things: evidence of effectiveness, economic assessment, and change management.

The evidence of effectiveness for NSAIDs is overwhelming when the test is comparison against placebo in acute or chronic conditions. But when it comes to which NSAID is the best in chronic conditions, we are in trouble. There are two Cochrane reviews of NSAIDs in hip and knee disease. That on osteoarthritis of the hip [3] found 43 randomised comparisons, but the lack of standardisation of case definition and outcome assessments, together with multiple different comparisons meant that no conclusions could be drawn about which NSAID was best. A systematic review of nabumetone [4] concluded that it had no advantages over other NSAIDs.

While accepting, then, that some patients may do better on one NSAID than another, if there is no clear difference in effectiveness, choice will be determined by safety and cost, and cost may be a real issue when the opportunities of health gains foregone because of higher cost prescribing are considered. An economic analysis of a single trial over only 12 weeks without significant differences does suggest some possible benefits for nabumetone [5], though it is heavily dependent on date from a few patients taking ibuprofen (2 patients with peptic ulcer bleeds out of 235) which looks out of line with longer-term and larger studies. Nor should we ignore the future, because in the next few years new entities which are likely to be much safer, but more expensive, are likely to become available, and then we will really have to think.

References:
1 AL Blower, A Brooks, CG Fenn et al. Emergency admissions for upper gastrointestinal disease and their relation to NSAID use. Aliment Pharmacol Ther 1997 11: 283-91.
2 CJ Hawkey, DJ Cullen, DC Greenwood et al. Prescribing of nonsteroidal anti-inflammatory drugs in general practice: determinants and consequences. Aliment Pharmacol Ther 1997 11: 293-8.
3 T Towheed, B Shea, G Wells, M Hochberg. Osteoarthritis: a systematic review of randomized controlled trials of analgesia and anti-inflammatory therapy in osteoarthritis of the hip. Cochrane Library 1997, issue 4.
4 SL Dahl. Nabumetone: a "nonacidic" nonsteroidal antiinflammatory drug. Annals of Pharmacotherapy 1993 27: 456-63.
5 RL Akehurst. M Backhouse, P Emery et al. An economic evaluation of nabumetone/reliflex compared with ibuprofen and a weighted NSAID combination. SCHARR Occasional Paper 96/2.

RELAX? - DON'T DO IT

Relaxation techniques have been used to produce freedom from anxiety and skeletal muscle tension, and there have been suggestions that relaxation techniques can be useful for relief of acute and chronic pain. Two excellent systematic reviews [1,2] indicate that, at best, this is not proven.

Both reviews used extensive searching techniques to establish that all published material had been found. Inclusion criteria were full journal publication, relaxation being used alone and not as part of a multimodal therapy, randomised studies, pain outcomes and numbers of treated patients no fewer than 10 per group.

Acute pain

There were seven studies with 362 patients, predominantly after surgery. Controls were generally non-treatment, waiting list controls, or use of music tapes. Three studies (61 patients received relaxation) showed significantly less pain with relaxation, while four (128 patients received relaxation) did not.

Chronic pain

Nine studies with 414 patients studied relaxation in chronic pain, seven in non-malignant pain and two in cancer pain. Controls were again of various types, including waiting lists or studies compared different relaxation techniques.

Three studies showed some efficacy for relaxation at early assessments, but none was effective beyond four months of treatment. In several instances control interventions (splints, hydro-galvanic baths or bio-feedback) produced lower pain scores than relaxation.

Comment

Evidence for the pain-relieving effects of relaxation is underwhelming. In acute pain, for instance, it was interesting to note that the studies with larger numbers tended to be negative while those with smaller numbers tended to be positive. Vote-counting of positive and negative studies has to be tempered by the ***weight*** of evidence, and here the weight of 3:4 against relaxation being effective on vote counting becomes 1:2 by using patients on active treatments. When we add the knowledge that there are instances of smaller trials tending to over-estimate treatment efficacy [3], the weight may become as high as 1:3 against or even more.

This is also an area where goalposts are easily moved: new method, technical expertise and so on. The fact is that although 16 randomised trials were found and evaluated, most were small, and few found any beneficial effect beyond that which might be obtained from taking a couple of aspirin.

Relaxation may still make people feel better. It was Earl St Vincent who said of Napoleon's invasion force " I do not say they cannot come, I only say they cannot come by sea". Perhaps of relaxation we can say that we do not deny that it may have a benefit, we merely say it does not relieve pain.

References:
1 K Seers, D Carroll. Relaxation techniques for acute pain management: a systematic review. Journal of Advanced Nursing 1998 27: 466-75.
2 D Carroll, K Seers. Relaxation techniques for chronic pain: a systematic review. Journal of Advanced Nursing 1998 27: 476-87.
3 RA Moore, D Carroll, PJ Wiffen, M Tramèr, HJ McQuay. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. British Medical Journal 1998 316: 333-8.

Book reviews

Practising Evidence-based Medicine. Sharon Strauss, Douglas Badenoch, Scott Richardson, William Rosenberg, David Sackett. Radcliffe Medical Press, Oxford, 1998. 80pp (email medical@radpress.win-uk.net).

This A4-format loose-leaf book is a seven session course for clinicians who want to learn more about the practical issues around incorporating critical appraisal of the best available evidence with their individual expertise. It complements other publications for the NHS Centre for EBM in Oxford. Because ***Bandolier*** is interested in diagnosis and test use, we turned to the example of an elderly woman with pneumonia and a low haemoglobin, and the use of a ferritin test in helping make a diagnosis.

We are provided with a step-by-step approach in which the clinical problem is outlined, with searching for evidence. The key papers are readily available in most libraries to be read with the example and worked through. There follows the "experts" answers. It was straightforward, sensible, and illuminating. It would make any of us more comfortable about tackling another such problem. The only thing we found strange was why, as it says in the book, it should take 10 days to obtain a ferritin result, for a test whose analysis time is measured in minutes or hours.

This is one of a series, and many people will benefit from these great tutorials for which there are learner and tutor manuals. The prices (for the complete, self-contained course) are: learners' and tutors' manuals at £25 each or a set of 10 learners with 1 tutor's manual for £200.

Statistical Issues in Drug Development. Stephen Senn. John Wiley & Sons, Chichester, 1997. 423pp, ISBN 0-471-97488-9, £50.

Now this book is not for the general reader, but it is a great book. ***Bandolier*** is beginning to worry about getting enthused by statistics books of late, but perhaps that marks a sea-change in the way they are written. Stephen Senn has a wry sense of humour, and a terrific turn of phrase that makes the book interesting - *"Statisticians know that words are important to statistics, yet surely their importance is not fully recognised"*; a quote from Kruskal in the Introduction which suggest that Senn, at least, has a real insight into the use and importance of words. Yes, there are lots of funny symbols in parts, but there is much wisdom without too much mining.

The first part of the book is given over to chapters of direct importance to clinical trials and drug development, and are of interest to any of us involved in designing, conducting, or interpreting clinical trial data. The brief history of medical statistics is also illuminating and interesting. For instance, Thomas Bayes' (of Bayes theorem) key work was published after his death by Richard Price. One of ***Bandolier***'s editors grew up in the same village in which Price was born - what are the odds of that happening?

The second part of the book is concerned with debatable and controversial topics in drug development. This includes topics like intention to treat, one and two sided tests, multi-centre trials and meta-analysis, and even includes a section of pharmacoeconomics. "*Pharmaco-economist: one who asks, not only if the treatment for dysentery was effective, but also after the price of toilet paper*." Senn scatters his book with fun quotes and jokes, and those of you who lecture often could do worse than get the book for these alone. They are ***very*** witty.

"*Ideally, nobody should study statistics who hasn't studied it already*". Senn's words, and wise ones. This book is one that many people involved in trials and use of evidence would profit by reading. It may not quite be something for the beaches of Spain, but it is very, very close to it. One final quote: "*Pharmaco-vigilance: a game of hunt the thimble, in which you are not sure if it is a thimble you are looking for, you don't want to find it anyway and the only time anyone shouts 'warm' is when you have already burnt your fingers*".

An evidence-based resource for pain relief. Henry McQuay and Andrew Moore. Oxford University Press, Oxford, 1998. 264pp, ISBN 0-19-262718-X. £65.

This A4-format book is written by two of ***Bandolier***'s editors, so it would be disingenuous to say more than what it contains. It draws together considerable work that has been going on for some years by researchers in Oxford and around the world in systematic review methods and results in pain relief. The question of which analgesic is the best in which particular pain context is one that has troubled researchers and clinicians for years, and still does.

The book is in three parts. The methodology - involving issues of validity and quality in pain trials, plus combining data - will particularly interest people doing trials and interpreting them. The sections on acute pain and chronic pain draw together a series of systematic reviews, with tables of all quality trials. Introductions and conclusions place the knowledge gained from the systematic reviews into clinical perspective.

Systematic Reviews. Synthesis of best evidence for health care decisions. Cynthia Mulrow and Deborah Cook. American College of Physicians, Philadelphia, 1998. 115pp. ISBN 0-943126-66-5. (no price available).

This is a collection of series of essays on systematic reviews published through 1997 in Annals of Internal Medicine for a general physician audience. They cover a range of issues, such as the synthesis of best evidence for clinical decisions, using systematic reviews in education and guidelines, and how consumers and policymakers can use systematic reviews.

The language is straightforward, and largely free of jargon. There are some interesting thoughts in these essays, and they contains some rules about how systematic reviews should be conducted and used.

Sophisticates will find some points with which to argue, but the book is a good introduction to systematic reviews - no, it is more than an introduction, perhaps an improvers primer, because most of us have by now been introduced to some of the basic concepts. The book (which is available through BMJ Publications) is useful for the departmental library shelf, and will be frequently consulted.

EVIDENCE-BASED EATING

Most people have a sense that eating whole-grain foods, like brown bread, cereals and pasta is a good thing. Putting a number on it is something else. A new meta-analysis [1] of case-control studies does just that.

Review

The researchers from Minneapolis used aggressive searching techniques to identify case-control studies which investigated the intake of whole grain foods and incidence of any cancer. They found 40 studies involving many thousands of patients and controls.

Results

Looking at instances where high versus low intake of whole grains was analysed or analysable, 43 of 45 instances in high quality studies had odds ratios of below 1, suggesting a positive association between whole grain food consumption and reduced risk of cancer. The pooled odds ratio for all cancers was 0.66 (95% confidence interval 0.60 to 0.72).

The findings were quite similar across all cancers. For individual cancers, the numbers of studies in which odds ratios were below 1 were:

- 9 of 10 in colorectal cancer or polyps
- 7 of 7 in gastric cancer
- 7 of 7 for hormone-related cancers
- 4 of 4 in pancreatic cancer
- 2 of 3 in brain cancer
- 8 of 8 for other cancers

Where pooled odds ratios could be obtained, most were in the range of 0.5 to 0.8, with only breast and prostate cancer having odds ratios close to 1 in a small number of studies.

There was a dose-response for intake (Figure). Compared with never eating whole grains, eating up to three servings a week reduced the pooled odds ratio to 0.82, while eating more than four servings a week reduced it to 0.59.

Comment

The implication of this analysis is that eating more than four servings of whole grain food a week reduces the chance of many cancers by about 40%. The effect in breast and prostate cancer is less. Of course, what we have here is an association, but the researchers examined all sorts of possible confounding variables, with little or no effect on the overall result.

Do we make enough of the information we have on lifestyles, and particularly eating habits, and their relationship to health? Telling people to eat brown bread is one thing, easily forgotten. Tell people, on the basis of good evidence in 40 studies with many thousands of people studied, that eating whole grains four times a week will reduce their risk of cancer by 40%, and emblazon it in clever television adverts, and ***Bandolier***'s guess is that habits could change.

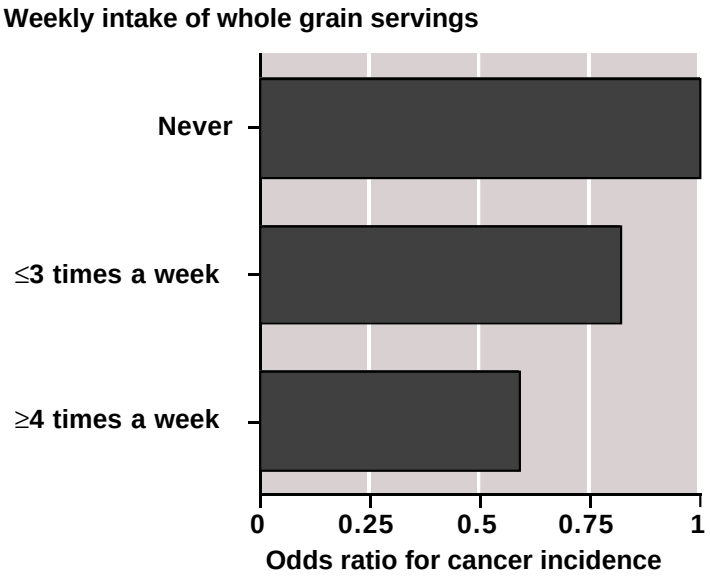
And it's not as if the evidence on lifestyle and health is bad news. Much of it is very good news indeed. In its pages over the years ***Bandolier*** has carried news on the lowering, dramatically, of the risk of stroke by eating a few vegetables, and on heart diease by taking a few alcoholic drinks, and on longevity by walking. Fish eating does great things as well. Many of these can be quantified, and people respond to numbers simply put, while not being lectured. It's time for a change in how we give people information about how to avoid seeing the doctor. Anyone out there want to sponsor a healthy living edition of ***Bandolier***?

It's all down to implementation. The landlady of a pub had diverticulitis, but the high fibre biscuits she was prescribed gave her wind. She put the biscuits on the bird table, with the result that customers' cars were covered in bird droppings and they couldn't see to go home. It brings a whole new meaning to outcomes research.

Reference:

1 DR Jacobs, L Marquart, J Slavin, LH Kushi. Whole-grain intake and cancer: an expanded review and meta-analysis. Nutrition and Cancer 1998 30: 85-96.

Dose-response for whole grain intake and cancer incidence



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